PROCEEDINGS OF

THE ROYAL SOCIETY.

Section B.—Biological Sciences.

The Microscopic Changes in the Nervous System in a Case of Chronic Dourine or Mal de Coit, *and Comparison of the Same with those Found in Sleeping Sickness.*

By F. W. Mott, M.D., F.R.S.

(Received February 21,—Read March 8, 1906.)

(From the Pathological Laboratory of the London County Asylums, Claybury.)

[Plates 1—4.]

Introduction.—I am indebted to Dr. Lingard, of the Imperial Bacteriological Laboratory of India, for the nervous tissues of an Arab stallion which acquired Dourine May 4 to 6, 1903. It exhibited 156 cutaneous plaques together with marked symptoms of paraplegia, and died August 15, 1905, 27½ months after infective coitus.

This disease, Dourine, is due to a specific form of trypanosome which has the power of penetrating the mucus membrane, affects equines, and is transmitted like syphilis by coitus. This is of especial interest, since Schaudinn has demonstrated the *Spirochæta pallida* of syphilis, particularly as it seems possible that trypanosomes may undergo a spirillar modification.

It is also of interest because, like some other trypanosome infections, it may, and frequently does, run a very chronic course and, as in the case under consideration, more than two years may elapse before a fatal termination. Again the lesion found in the lumbo-sacral region of the spinal cord presents some points of resemblance to a localised syphilitic meningo-myelitis.

A comparative examination of the nervous tissues in this disease with that of animals infected with *Trypanosoma Gambiense*, and with the tissues of human beings dying of chronic Sleeping Sickness, especially those in which there was no evidence of terminal or secondary microbial infection, is of interest in showing that prolonged trypanosome infection causes in all three conditions a marked proliferation and overgrowth of the subpial, septal, and perivascular neuroglia tissue. A chronic interstitial inflammation of the connective tissue structures with lymphocyte infiltration occurs, owing to the presence of an irritative agency in the lymphatic system, which, in the case of Dourine, starting in *one* seat of primary infection, extends to the inguinal glands, thence presumably by the pelvic lymphatics to the lumbo-sacral plexus and the posterior lumbo-sacral roots to the central nervous system; consequently the lower part of the spinal cord and especially the posterior column is first and most affected. In the case of Sleeping Sickness there may be any number of seats of infection, but the cervical glands are nearly always markedly involved.

Material and Notes of Case.—The following portions of the central nervous system of the stallion, hardened in Formol-Muller solution, were examined by various methods to display the neural and neuroglial structures. (1) Brain, lateral side of left lobe. (2) Portion of cervical spinal cord, between third and fourth cervical nerves. (3) Portion opposite the 19th nerve (12th dorsal). (4) Portion taken midway between the 22nd and 23rd pair of nerves (15th and 16th dorsal). (5) Portion with 30th pair of nerve roots attached.

The notes accompanying these tissues were as follows :—

An account of the Arab stallion (Monarch) will be found in the Appendices, "Report on Dourine in Different Breeds of Equines, etc.," by Alfred Lingard, M.B., M.S., D.P.H., Imperial Bacteriologist to the Government of India. Page 21.—Infective coitus occurred on May 4 to 6, 1903. Eruption of 156 cutaneous plaques, between June 6, 1903, and August, 1905. Partial paraplegia appeared February 25, 1904. Death (836th day) August 15, 1905.

Post-mortem.—A considerable quantity of gelatinous exudation was found round the lumbar portion of the spinal cord, and a smaller amount around the cervical enlargement, and a certain quantity of cerebro-spinal fluid escaped from within the membranes on removal.

The cerebro-spinal fluid did not exhibit the *Trypanosoma Equiperdum* when searched for in numerous stained specimens.

Previous Observations on the Changes in the Nervous System in Dourine.

It is unfortunate that nerves of the hinder extremities were not sent, for Laveran et Mesnil* thus refer to the histological examination by Marck: "He showed a degeneration of the nerve fibres of the posterior columns; the other parts of the spinal cord (grey substance and other bundles of white substance) are in a healthy state. Some nerve fibres, especially on the sensory side, are degenerated at different points; the nerves of the fore-limbs are less altered. Having ascertained these facts Marck calls Dourine infective polyneuritis of the horse."

Methods of Examination.—Some portions of the tissues were embedded in paraffin and sections cut 10 μ thickness and stained by the following methods:—Polychrome and Eosin, Azure Blue, Van Gieson and Leishman's stain. Other portions were embedded in celloidin and sections of 20 μ thickness were cut and stained by the new Weigert method, modified Mallory and by Van Gieson's fluid. The sections by this method were thicker, but I was enabled to obtain sections of uniform thickness of the cord and membranes together with the roots, inflammatory material and attached vessels.

Description of Histological Changes in Dourine.

Throughout the grey matter of the spinal cord the ganglion cells show marked chromolytic changes and the vessels exhibit evidence of chronic inflammation with scattered capillary hæmorrhages.

The small vessels show lymphocyte infiltration around, but there is nothing resembling the marked perivascular lymphatic infiltration met with *throughout* the grey matter in all cases of well-marked Sleeping Sickness. The ganglion cells for the most part retain their normal outlines, but are stained a uniform bluish purple with a badly defined and imperfectly stained pattern of Nissl granules. (*Vide* Photomicrograph 1.) The most marked change is observed in the lumbar region.

Sections of the lumbo-sacral cord with attached roots, after embedding in celloidin and staining with Van Gieson's fluid and by the Weigert method, exhibited the following changes. The roots, anterior and posterior, are infiltrated with lymphocytes, also all the vessels are surrounded and their walls infiltrated with small round cells. The connective tissue septa carrying the vessels as well as the perineurion and endoneurion are thickened and infiltrated with lymphocytes, also the loose connective tissue outside the dura mater; the dura mater itself and the vessels and tissues in the subdural space show signs of chronic inflammation. The condition simulates an

* 'Trypanosomes et Trypanosomiasis,' p. 283.

acute syphilitic meningitis in many ways, except that I can discover only occasional evidence of an obliterative arteritis. (*Vide* figs. 1 and 2, Plate 2 and Photomicrograph 12.)

Some of the larger roots seen in the section (*vide* Photomicrograph 7) are very markedly affected by the inflammatory process. These are judged to be posterior roots, because a posterior spinal ganglion cell can be seen here and there in them; moreover, they occupy among the roots a posterior position. The capsules of the ganglion cells that are seen are crowded with lymphocytes presenting an appearance like that observed in Sleeping Sickness. Some of these roots in transection under a high power show the nerve fibres to have been destroyed and their place occupied by proliferated branching neurilemmal connective tissue cells lying in the centre of an oval or circular space bounded by highly vascular thickened, and swollen and amorphous endoneurion. In the centre of most of these cells is a highly refractive round or oval space. (*Vide* fig. 6, Plate 1.)

Throughout the spinal cord, but especially at the lumbo-sacral and cervical enlargements, there is a marked thickening of the subpial network of the glia tissue which extends into the white substance along the main septa and branches. (*Vide* Plate 2, fig. 2.)

At the periphery the proliferated glia tissue consists mainly of a dense reticulum of fibrils, but in the substance of the white matter great numbers of large branching neuroglia cells are seen sending their processes in all directions. On careful examination of the longitudinal and transverse sections (*vide* Photomicrographs 5 and 6), these proliferated neuroglia cells, which are often spoken of as mesoglia cells, can be seen to send their processes to end like a foot upon the wall of a small vessel. This overgrowth of glia tissue is seen throughout the white matter of the spinal cord whatever region is examined, but more especially in the lumbar and cervical enlargements, especially the former. It is more obvious in the posterior columns than elsewhere, especially along the median fissure and in the root zone. It does not *wholly* correspond to system tracts of fibres which have undergone degeneration, but appears (except in the root zone of the posterior column) to be a chronic formative proliferation of the glia tissue caused by an irritant entering the lymphatics and subarachnoid space. The posterior column is much more affected than the rest of the white matter.

In the lumbo-sacral region there are three definite zones of degeneration in the posterior column, no doubt corresponding to the destroyed roots. (*Vide* Photomicrograph 8.) The lymphocyte infiltration is observed around the small vessels and numerous lymphocytes are scattered about in the septa of the white matter. In the roots a well-marked perivascular infiltration

with lymphocytes can be seen and some hæmorrhages in the lumbar region. The chronic interstitial inflammation of the anterior roots, in which all the nerve fibres appear to be normal, together with the fact that there is subpial proliferation of the glia tissue of the lumbo-sacral and cervical enlargements in their entire circumference, with extension of the same along the septa, shows that this proliferation of the connective tissue supporting structure, whether of the undamaged roots or of the spinal cord, is not due to atrophy of the nervous elements; although in the posterior columns where there are three definite bands of sclerosis the neuroglial proliferation is without doubt secondary to neural destruction. (*Vide* Photomicrograph 3.) Occasional foci of micro-organisms are seen, but do not play any part in the *chronic* changes above described. They are not found in the blood or inflammatory exudations. In none of the sections could I find any trypanosomes stained by the various methods, which we know will show them, if they are present in any numbers. Since the above description was written I have received from Dr. Lingard the remainder of the central nervous system, including a number of the spinal ganglia. *I was thus enabled when reading the paper at the Royal Society on March* 8 *to communicate the following additional facts,* which have, I consider, an important bearing upon the degeneration of the posterior roots and the sclerosis in the posterior columns. The facts which will be now stated may also explain some of the characteristic symptoms of the disease and afford some further evidence of similarity to Sleeping Sickness in the morbid change occasioned by chronic trypanosome infection.

Sections of the posterior spinal ganglia and attached roots in the cervical, upper dorsal, mid dorsal, lower dorsal, and lumbo-sacral regions have been examined by the methods previously described and the appearances compared with those observed in Sleeping Sickness. In all these ganglia there was evidence of intense chronic inflammation with marked proliferation of the endothelial nuclei of the capsule and lymphatics, together with lymphocyte infiltration of the interstitial fibrous tissue, and this morbid change can be followed from the nerves to the ganglion and along the posterior roots. This change is most marked in the lower dorsal and lumbo-sacral ganglia, and where the chronic inflammation is most intense, there the posterior spinal ganglion cells are most affected. In all the sections some of the ganglion cells have undergone vacuolar degeneration, and even complete destruction, their place being occupied by inflammatory products (*vide* Photomicrograph 4), but the neuronic destruction is most marked in the lumbar region, which is the situation, as before remarked, of extensive posterior root destruction and system-degenerative sclerosis of the posterior columns. (*Vide* Photomicrograph 3.)

Both these conditions are the outcome of the destruction of the posterior spinal ganglion cells. But this destruction must also have led to destruction of the peripheral branch of the T-shaped process of the ganglion cells, and this would give rise to a sensory polyneuritis. Unfortunately, I have not had forwarded to me any of the nerves to examine. However, the comparatively normal appearance of the anterior roots, and the very complete destruction of many of the sensory roots, together with the well-marked sclerosis of the posterior columns, would suggest that this animal may have suffered with a sensory paralysis of the hind limbs analogous to tabes dorsalis, rather than a polyneuritis. An argument in favour of this hypothesis is that in severe alcoholic and other forms of polyneuritis the motor anterior horn cells usually show characteristic degenerative changes which are not seen in the spinal cord of this animal. Now it has been shown by numerous authorities, but especially in a very systematic manner by Head and Campbell, that herpes zoster is caused by an inflammation of the posterior spinal ganglia, the seat of the eruption depending upon the particular segmental ganglion or ganglia affected. It is therefore reasonable to associate the eruption of the characteristic cutaneous plaques with the inflammatory irritation of the ganglia as they become successively affected by the noxious agent.

Both Lingard and Laveran remark upon the curious nature of the eruption: the former believes it to be an angio-neurotic œdema which occurs in the form of circular plaques, as if a ring had been introduced under the skin. They remark that although trypanosomes can only be found in the blood with difficulty, yet they are always present in the fluid which can be drawn from a plaque. Lingard concludes therefore that embolism by trypanosomes is the cause, but if there is an angio-neurotic œdema occasioned by the irritation of the posterior spinal ganglia, then it is possible that in the blood or the inflammatory exudation the trypanosomes may find suitable conditions for multiplying by fission. The theory which I have advanced for the origin of the rash finds some support, moreover, in experiment, for Dr. Bayliss has shown that stimulation of the posterior roots produces vaso-dilation. Again, these plaques often leave patches of leucoplacia which may be due to neurotrophic causes associated with the destruction of numbers of the spinal ganglion cell neurotrophic centres.

In chronic trypanosome infections by *T. Gambiense*, even before the lethargy occurs, outbursts of irritative papules or other skin eruptions occur, and they might be accounted for by irritation of the neurotrophic centres in the spinal ganglia. The changes in the ganglia are never so intense as in

Dourine, but I have now examined quite a number of posterior spinal ganglia in Sleeping Sickness cases, and I have never failed to find some change, never sufficient, however, to produce cell destruction, such as is found in Dourine. The most intense change I have met with is shown in Photomicrographs 7 and 8, and this in no way differs, except in degree, from that seen in Dourine.

Laveran and Mesnil mention that dislocation and fractures may occur in Dourine, and we know that spontaneous dislocation and fractures are met with in tabes dorsalis, a disease in which the posterior roots and posterior columns of the spinal cord undergo degenerative atrophy.

The membranes at the base of the brain of this animal, which died of Dourine, seemed thicker than normal. On microscopic examination sections of the peduncles and interpeduncular structures exhibited a subpial and septal neuroglia proliferation very similar to that seen in the lumbar region of the spinal cord. I observed, however, but little or no lymphocyte infiltration.

Comparison of the Changes in the Tissues of Animals Dying after Inoculation with Trypanosoma Gambiense, *also with the Tissues of Human Sleeping Sickness, with those met with in the Case of Dourine above described.*

The examination of the tissues of the spinal cords of a number of cases of Sleeping Sickness, especially of several chronic cases in which there was no terminal or secondary infection from suppurating glands, shows a glia proliferation in the spinal cord and throughout the nervous system similar to that above described, and it may be remarked that the lymphocyte proliferation is not always in proportion to the glia proliferation. Moreover, in all chronic cases there is a marked glia proliferation around the central canal of the cord.

Zururu bin Mza and Masake* were very chronic cases in which there was a most extensive glia proliferation certainly not all due to secondary degeneration, but caused by a chronic interstitial inflammatory extension along the subpial septa and perivascular spaces (*vide* figs. 1 and 2, Plate 1) without marked destruction of the intervening nerve fibres.

"Cases of two monkeys inoculated with *Trypanosoma Gambiense*"†:—

(1) A monkey infected by fresh fly feeding, the animal dying eight months later. No perivascular lymphocyte infiltration was discovered in the central nervous system, but there was a very marked chromolytic change in the ganglion cells of the medulla, also a considerable degree of acute glia cell

* *Vide* 'Reports of the Sleeping Sickness Commission,' No. VI, pp. 270 and 234.

† *Vide* 'Reports of the Sleeping Sickness Commission,' No. VI.

proliferation. There was also in the subjacent cortical white matter a perivascular glia proliferation. (*Vide* figs. 3 and 4, Plate 1, and Photomicrograph 12.)

(2) The monkey dying eighteen months after inoculation with *Trypanosoma Gambiense*, in which the lesion of Sleeping Sickness was found by Major Leishman and described by Captain Harvey.*

I have found in portions of the brain of this animal (kindly given to me by Major Leishman) a profound neuroglia proliferation, similar to that seen in Dourine and chronic Sleeping Sickness. The lymphocyte proliferation is not very marked, and the cellular proliferation in the perivascular lymphatics is in many parts due more to neuroglial proliferation than lymphocyte infiltration. Photomicrograph 11 and fig. 5, Plate 1, show this proliferation in the sheath of a vessel which has been cut longitudinally. This seems to indicate the pathology of the process, viz., the overgrowth of the perivascular glial tissue meshwork, which stops the proliferated lymphocytes, and leads to their accumulation in the perivascular sheath.

Conclusions.

The more chronic the case of trypanosome infection, the more extensive is the glia cell proliferation. The overgrowth of glia tissue is manifested by an increase in number and size of cells and fibrils. Many large cells are seen, with branching processes, sending one process to form a foot on the vessel wall, others are seen entering into the formation of a dense reticulum in the perivascular lymphatic space. (*Vide* Plate 1, figs. 1 and 5, and Photomicrographs 10, 11, 12.) Normally, the perivascular spaces have only a few delicate septa passing across, which could not in any way impede the flow of the cerebro-spinal fluid and lymphocytes.

Dr. Eisath, working in my laboratory, has recently shown by a differential method of staining that a large number of the round cellular elements contained in the perivascular infiltration of chronic Sleeping Sickness are not lymphocytes, but the nuclei of neuroglia cells. I have not found this glial proliferation in acute cases of trypanosome disease of animals, only in the chronic case of Dourine, and in the two cases of experimental Sleeping Sickness in monkeys above referred to. The glial proliferation in these cases is in excess of, and appears to precede, the perivascular lymphocyte accumulation so constantly found in human Sleeping Sickness, which we now know may be a very chronic disease. Moreover, in most cases of uncomplicated

* "Report on a Case of Experimental Sleeping Sickness in a Monkey, *Macacus rhesus*," 'Journal of the Royal Army Medical Corps,' No. 5, vol. 4.

human Sleeping Sickness, there is in the spinal cord a universal proliferation of the glia tissue extending along the subpial septa and vessels, without apparently destroying the nerve fibres. (*Vide* Photomicrograph 9.)

It is possible, therefore, that the lymphocyte accumulation in the perivascular lymphatics does not occur until the neuroglia proliferation has become advanced, and this may account for the fact that leptomeningeal perivascular infiltration with lymphocytes (so-called chronic meningo-encephalitis) is not met with in the nervous tissues of animals inoculated with various trypanosomes, that die within a comparatively short time, either from exhaustion, or from the poisonous effects of the infection upon the cells of the nervous system or from secondary microbial invasion.

Greig* concludes from his experiments that the onset of the symptoms of Sleeping Sickness synchronise with the entrance of the trypanosomes into the lymph spaces of the nervous system, and this is accompanied by an increase of lymphocytes in the cerebro-spinal fluid. Whether it be as Greig's experiments suggest, that the continuous presence of the trypanosomes in the cerebro-spinal fluid acts as a direct cause of irritation of the lymphatic structures of the central nervous system; or whether it be the result of the absorption of toxic products from the multiplication of the trypanosomes in the lymphatic glands; or whether it be the extension of a chronic inflammatory process from the paravertebral glands along the lymphatics of the vessels and nerves proceeding to the cerebro-spinal axis, as seems probable in Dourine, one fact is certain, and that is, the symptoms of Sleeping Sickness are associated with, and the depth of the lethargy and chronicity of the disease is in great measure proportional to, the extent and degree of leptomeningeal, septal, and perivascular lymphatic cell proliferation. This cell proliferation is made up partly by an overgrowth both in number and size of the neuroglial cells to form a dense meshwork and partly of accumulated entangled and occasionally altered lymphocytes. In proportion to this chronic lymphatic inflammation the neural elements display relatively slight degenerative changes in cases uncomplicated by microbial infection; thus differing from Dourine, where there was very obvious degeneration of posterior spinal ganglion cells and roots with corresponding degeneration in the posterior column.

The mind of a patient suffering with Sleeping Sickness remains clear usually until near the end. He can easily be aroused from his lethargy, and comprehends what is said to him, replying in a slow, sleepy manner, and with manifest disinclination to continue a conversation, or to exercise any mental or bodily effort. These symptoms point to a functional depression of the anatomical basis of the seat of consciousness rather than to a widespread

* 'Reports of the Sleeping Sickness Commission,' Vol. 6.

destruction as in general paralysis of the insane. This functional depression of the neural elements may be accounted for, by (*a*) increased intracranial pressure brought about by the retardation of the lymph circulation and the cell proliferation; (*b*) the interference with the blood circulation, and with the gaseous and metabolic exchanges between the blood and the lymph, and between the lymph and the neurone; (*c*) in chronic cases by a certain amount of neurone destruction as shown by Marchi's degeneration of fibres, and a certain amount of cell and fibre destruction.

DESCRIPTION OF PLATES.

Plate 1.

In these figures only the neuroglial tissue is shown. Magnification ×500.

Fig. 1.—Proliferating branching glia cells in the subpial tissues of the cortex in a case of very chronic uncomplicated human Sleeping Sickness. (Masake, 'Sleeping Sickness Reports,' vol. 6, p. 234.)

„ 2.—Extension of the proliferated glial tissue along a septum of the spinal cord, showing the processes of the glial cells extending on to a small collapsed vessel (Masake, 'Sleeping Sickness Reports,' vol. 6, p. 234.)

„ 3.—Various stages in acute glial cell proliferation, seen abundantly in the brain tissues of the monkey, dying eight months after infection by fresh fly feeding. Lymphocytes (*l*) are also seen.

„ 4.—Ditto with branching glial cells, their processes enveloping and extending on to a wall of a small vessel.

„ 5.—Very marked glial proliferation around a small vessel. The cells are older, being much larger and their processes more numerous and extensive. A long process can be seen extending from the large branching neuroglial cell and terminating in a foot on the wall of the vessel. This represents the glial proliferation found in a monkey which died with lesions similar to human Sleeping Sickness. These drawings were made from preparations of 10 μ thickness, stained by polychrome and eosin method. The body and processes of the neuroglial cell stain pink, the nucleus purple.

„ 6.—Section of degenerated root of 30th segment of the spinal cord dourine, stained by Van Gieson's method.

All the nerve-fibres have disappeared. Preparations stained by Weigert method show that nearly all the fatty matter has been absorbed; the axis cylinders have disappeared and no regeneration has occurred. The endoneurion is highly vascular, proliferated, and increased in amount. The circular spaces corresponding to the degenerated nerves are still seen, but no nerve-structure is left. The clear space seen in the centre of the enlarged neurilemmal cell corresponds to the space formerly occupied by the axis cylinder and its coating of myelin. From its colour and high refraction, it is probably filled with fat.

Plate 2.

Fig. 1.—Drawing of the inflammatory exudation around 30th segment of the lumbo-sacral spinal cord, with attached membranes and roots, Dourine. Stained by Van Gieson's method. Magnification ×230.

R, Periphery of root with lymphocyte proliferation of very much thickened perineurion (I).

The nerve-fibres appear to be intact.

A, Two small arteries with obliteration of lumen by inflammatory thickening of their walls. Beneath there is a quantity of loose fibrous and gelatinous material with cell nuclei.

G, Posterior spinal ganglion cell with nuclear proliferation of the capsule and leucocytes.

L, Leucocytes.

Fig. 2.—Adjacent portion of the lateral column of the spinal cord, showing a leptomeningitis with great thickening of the subpial neuroglia tissue and extension of the same along the septa. Photomicrograph 6 shows the appearance presented where this was cut longitudinally. Extending from the main septa are branching septa consisting of neuroglia cells. Many of these neuroglia cells, with distinct nuclei and branching processes running round and between the nerve-fibres, can be seen. In this case the noxious agent which has caused this change has operated from the sub-arachnoid space and proceeded inwards along the lymphatics of the septa.

The drawings have been made by Miss Agnes Kelley and are faithful reproductions of the appearances presented by the specimens.

DESCRIPTION OF PHOTOMICROGRAPHS OF DOURINE.

Plate 3.

1.—Anterior horn lumbo-sacral region. The motor spinal cells show a diffuse stain, indicative of a slight coagulation necrosis. The outline of the cells is not altered much. There is a general proliferation of the glia cell nuclei and a lymphocyte infiltration, not pronounced around the capillaries and small vessels. Polychrome eosin stain. Section 10 μ thickness. Magnification $\times 180$.

2.—Section of posterior root of 30th segment, showing degenerative atrophy of the nerve-fibres, inflammatory change in the sheath around and proliferation of the cells of the perineurion and endoneurion. Polychrome eosin stain. Sections 10 μ thickness. Magnification $\times 120$.

3.—Section of the posterior column, showing three bands of degenerative sclerosis in the root zone. Weigert stain. Celloidin preparation.

4.—Section of posterior spinal ganglion, lumbo-sacral region. Van Gieson's stain. Showing chronic inflammatory change with atrophy and destruction of the ganglion cells. Magnification $\times 200$.

5.—Section of lateral column 30th lumbar segment, showing septal proliferation of the glia cells without destruction of the intervening nerve-fibres. Van Gieson's stain. Magnification $\times 150$.

6.—Longitudinal section of the subpial tissue of the 30th lumbar segment, showing neuroglia proliferation. Eisath's stain. Magnification $\times 850$.

PLATE 4.—SLEEPING SICKNESS.

7.—Posterior spinal ganglion, case of chronic Sleeping Sickness, showing wide-spread interstitial chronic inflammation. Polychrome eosin stain. Section 10 μ thickness. Magnification $\times$85.

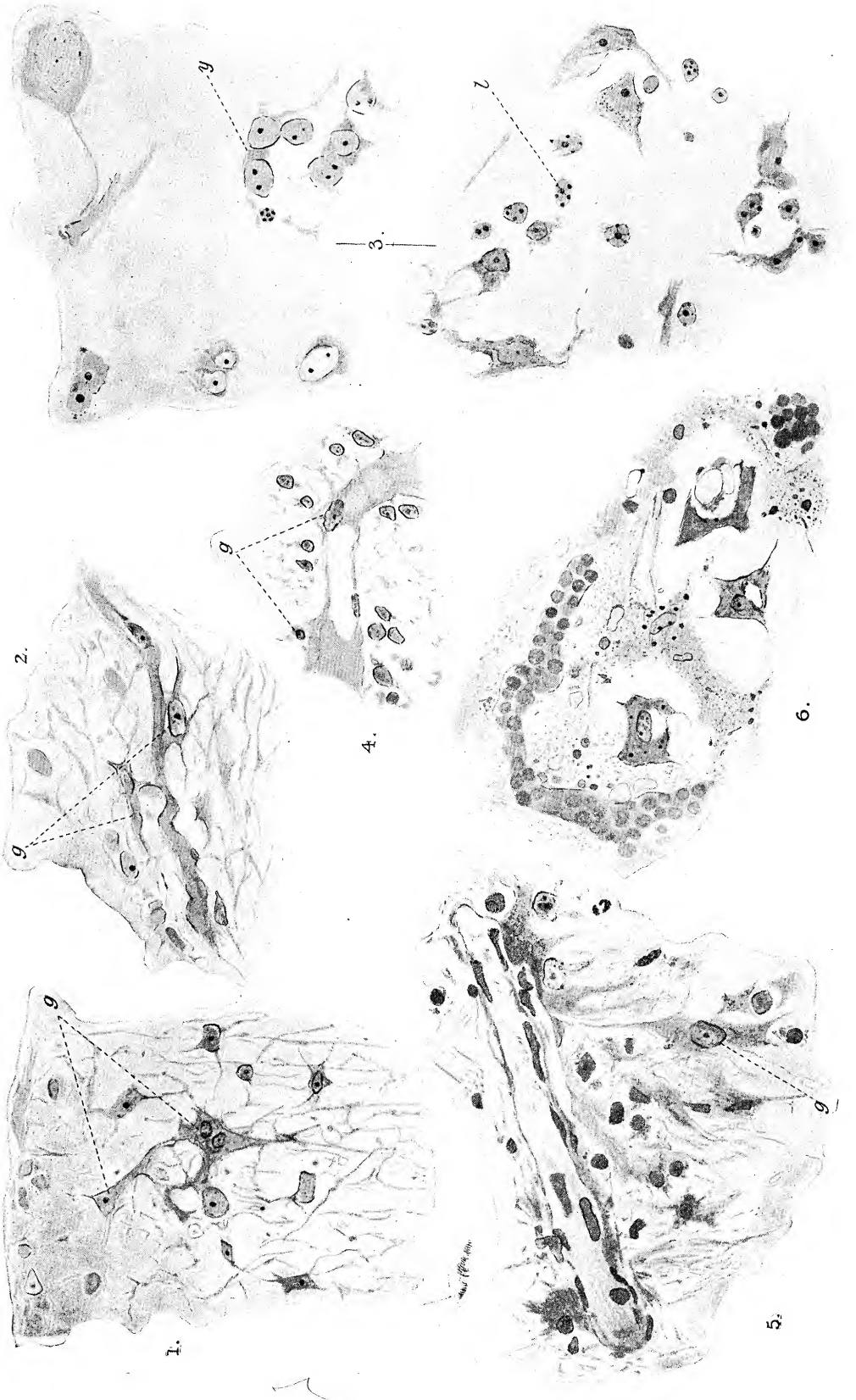
8.—Ditto. Magnification $\times$480. Showing the proliferation of the endothelial cells of the capsule and lymphocyte interstitial infiltration.

9.—Section of the spinal cord, chronic Sleeping Sickness, showing septal glia proliferation, partly due no doubt to degenerative atrophy of the nerve-fibres. Weigert stain. Sections 30 μ thickness. Magnification $\times$80.

10.—Section of a vessel with surrounding lymph space, chronic Sleeping Sickness. A meshwork of fibrils is seen, derived from the branching processes of the neuroglial cells. The neuroglia nuclei are stained, the lymphocytes are unstained. Magnification $\times$480.

11.—Vertical section of a perivascular space in the brain of the monkey which died of chronic Sleeping Sickness. Material kindly given by Major Leishman. Stained by polychrome eosin. Three large neuroglia cells, with branching processes, are seen, and many others in parts. Entangled in the meshwork are numerous lymphocytes. Magnification $\times$ 600.

12.—Section of monkey's brain infected with *T. Gambiense*, showing glia cell proliferation. Many of the glia cells can be seen with their processes extending on to the wall of the vessels. There is a glia cell nuclear proliferation also. Heidenhain, eosin stain. Magnification $\times$ 250.


y
3.
z
g
4.
2.
g
6.
g
1.
5.

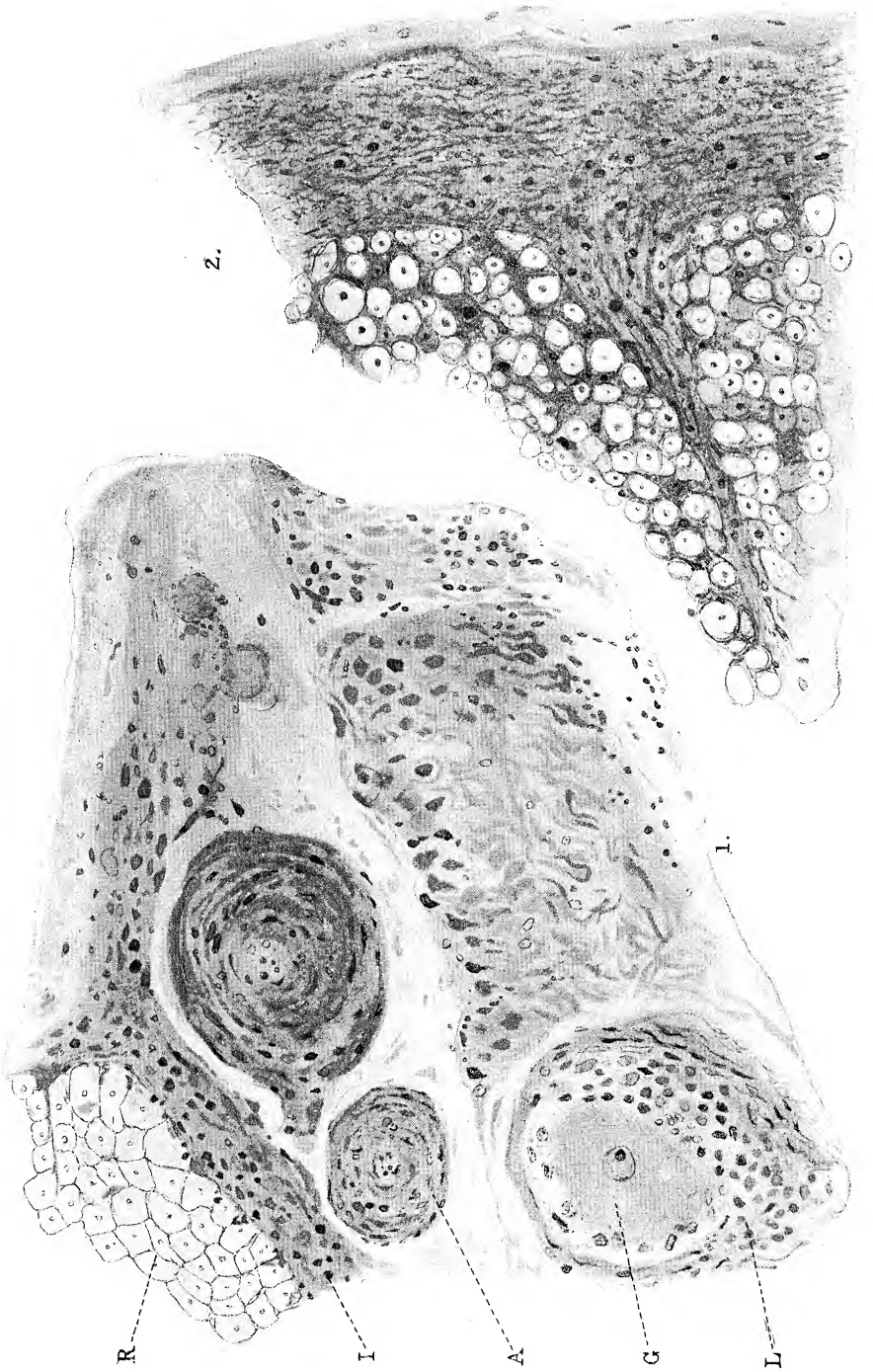

2.
1.
R
I
A
G
L

FIG. 1.

FIG. 2.

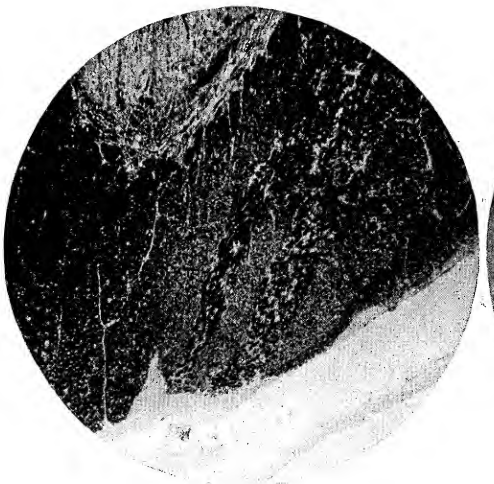


FIG. 3.

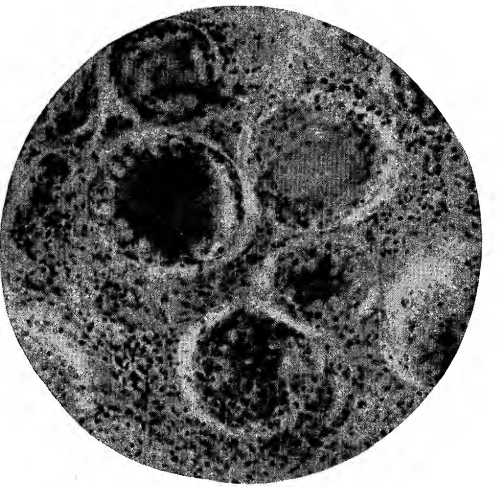


FIG. 4.

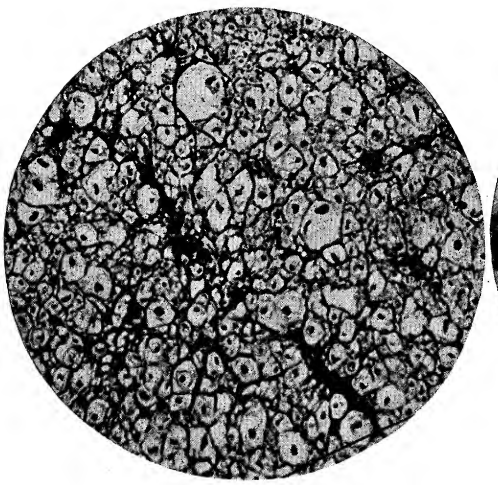


FIG. 5.

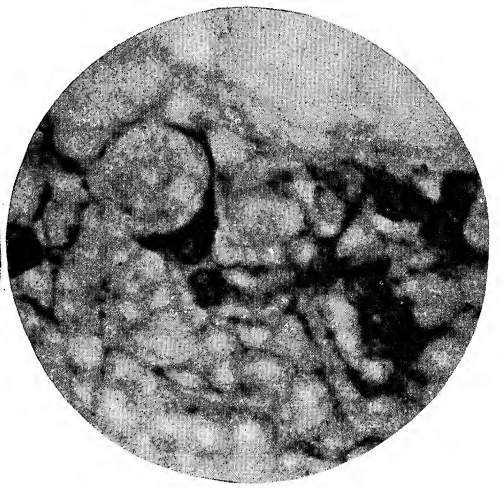


FIG. 6.

FIG. 7.

FIG. 8.

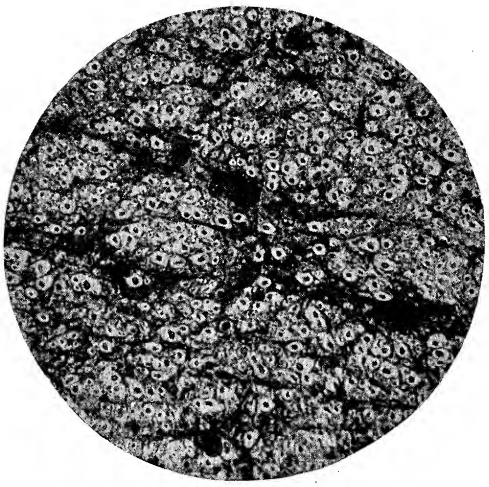


FIG. 9.

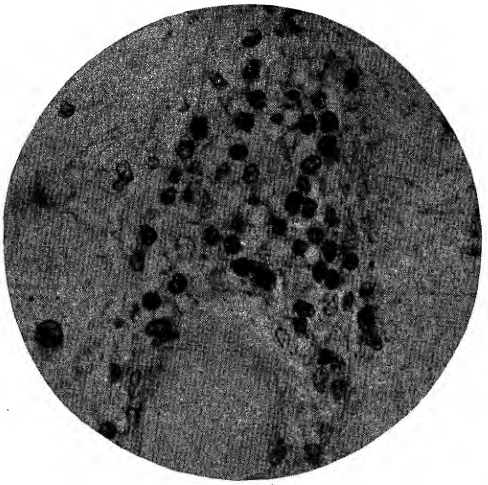


FIG. 10.

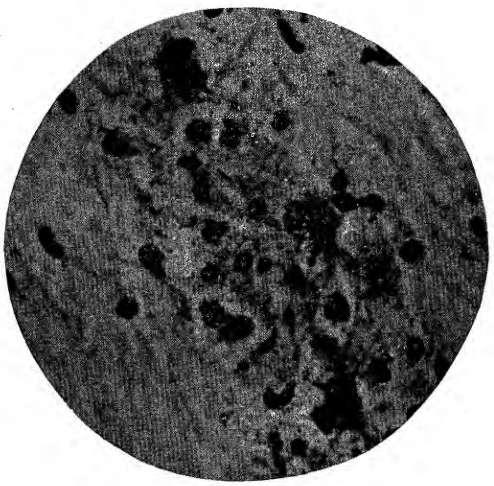


FIG. 11.

FIG. 12.


1.
g
2.
g
3.
y
l
4.
g
5.
g
6.

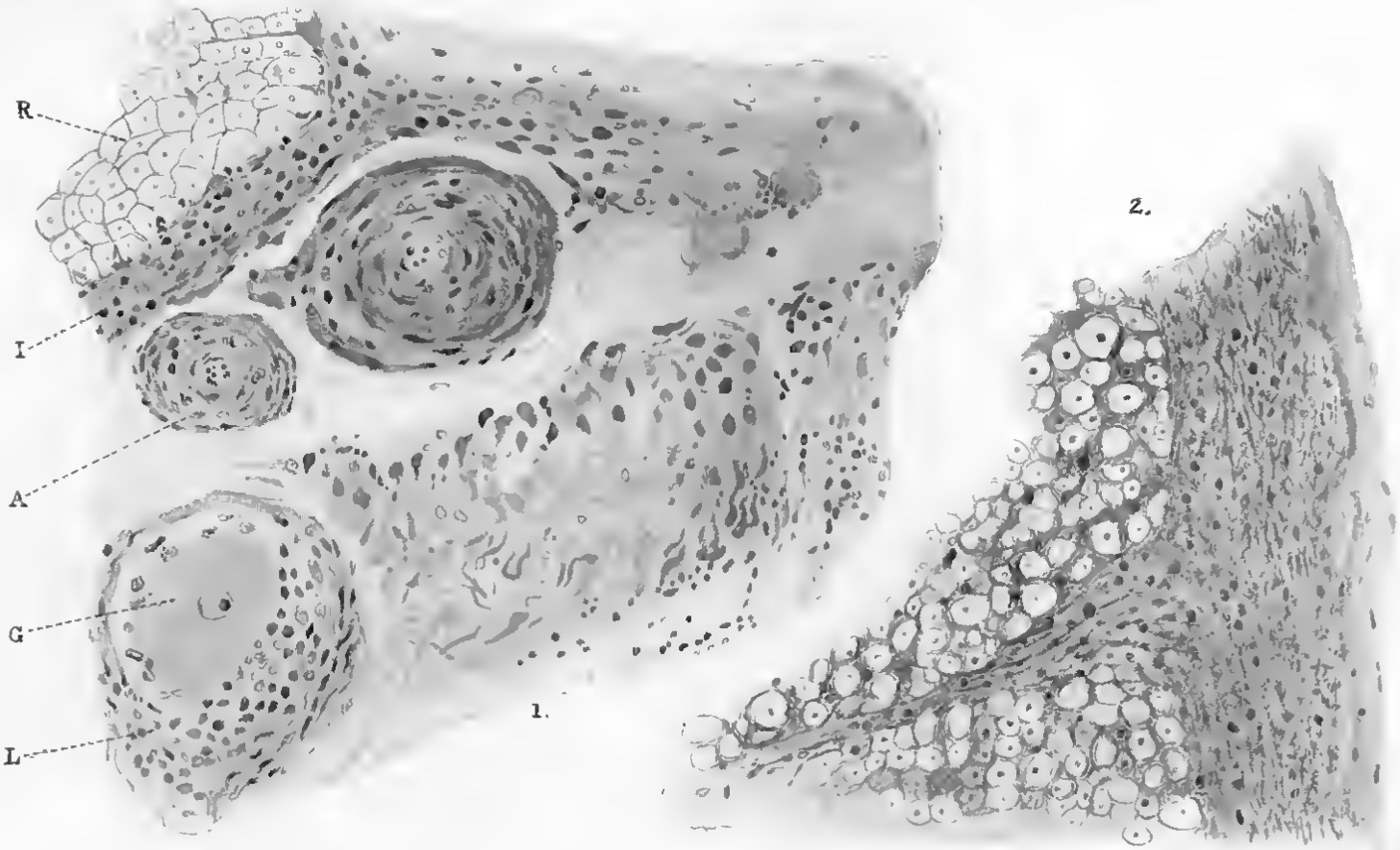

R
I
A
G
L
1.
2.

FIG. 1.

FIG. 2.

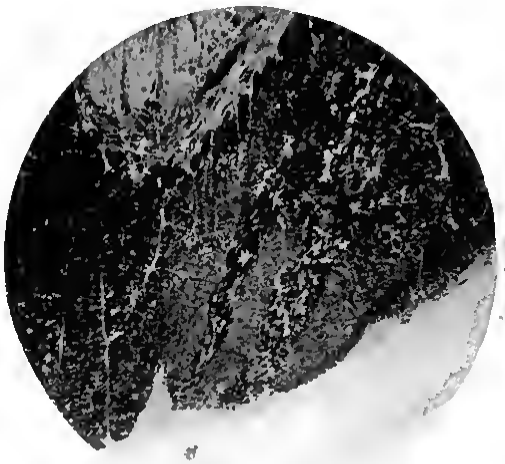


FIG. 3.

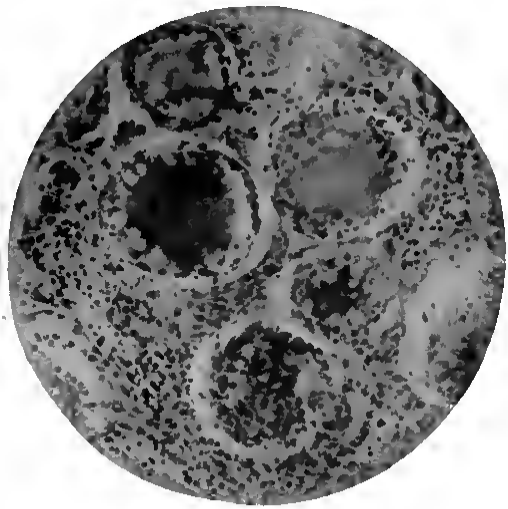


FIG. 4.

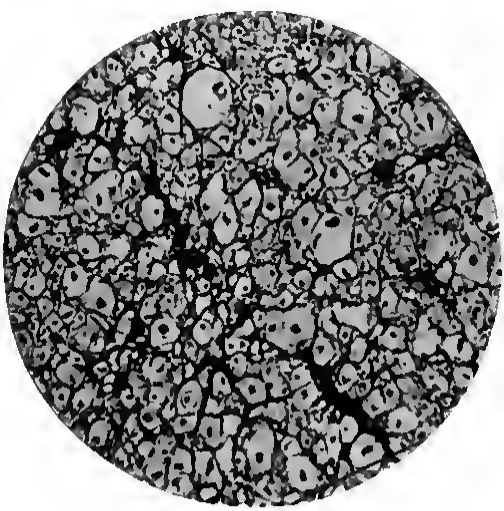


FIG. 5.

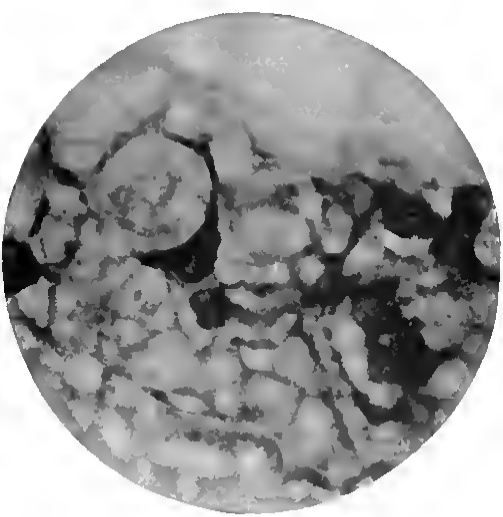


FIG. 6.

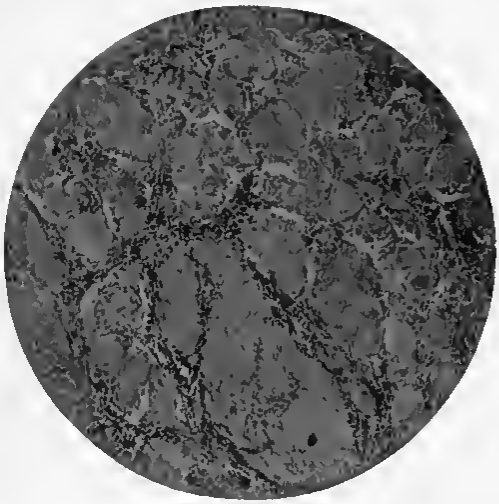


FIG. 7.

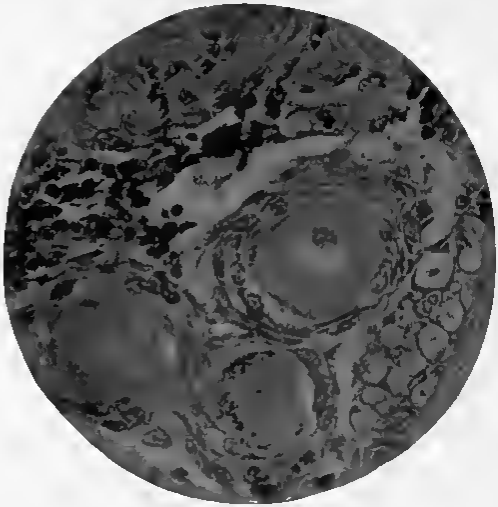


FIG. 8.

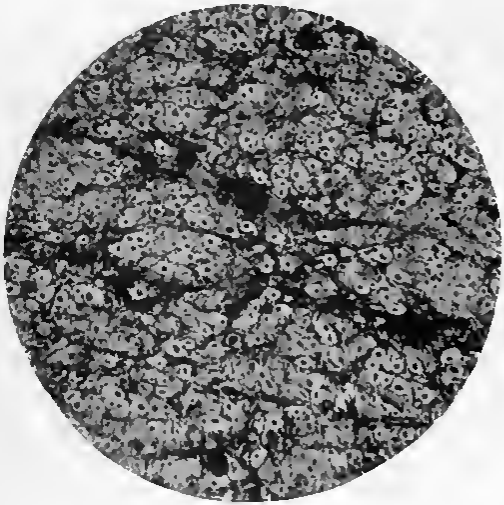


FIG. 9.

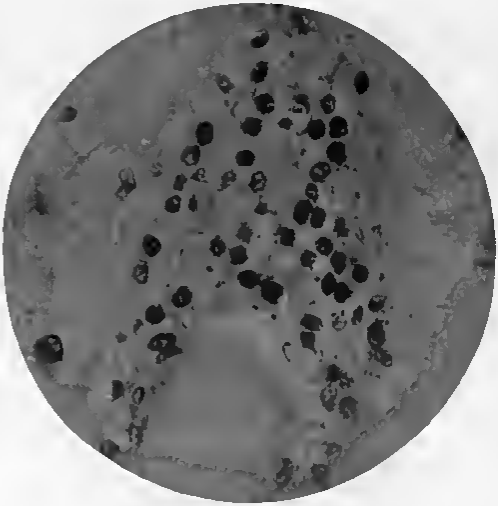


FIG. 10.

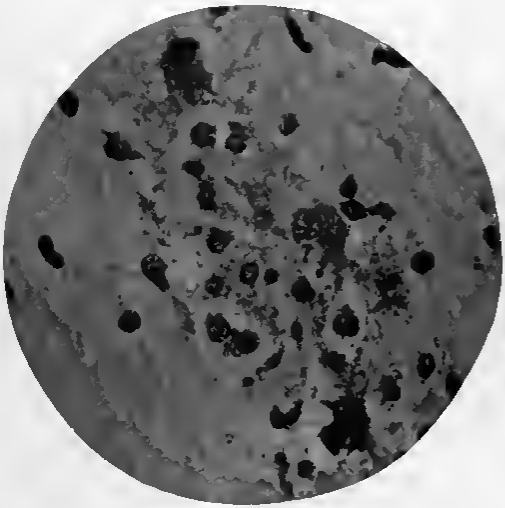


FIG. 11.

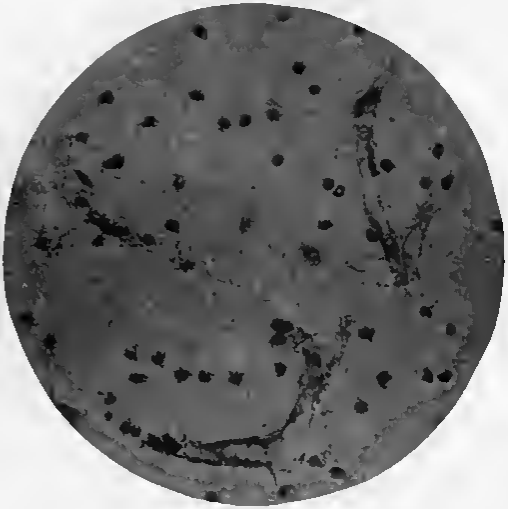


FIG. 12.